REMARKS

Objections to Specification

The disclosure was objected to for failure to capitalize all of the letters in the trademark "FACSTAR PLUS" and to utilize the generic terminology. An appropriate amendment has been made above.

Rejections Under 35 U.S.C. § 102

Claims 13-14 and 17-24 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Flamand et al. as evidenced by Unanue and Dezutter-Dambuyant. This rejection is respectfully traversed.

Flamand is cited as teaching *in vitro* incubation of murine dendritic cells with tumor specific antigens from murine BCL1 lymphoma cells. The resultant "product" produced by this method is an antigen pulsed dendritic cell. Significantly, as conceded in the Office Action, the dendritic cell is pulsed only with a *specific* antigen. As a result, the dendritic cell only elicits an antibody response to a specific tumor challenge; in other words, pulsing with the BCL1 antigen only provides protection against a BCL1 challenge. Thus, the method taught by Flamand requires isolation and identification of a particular antigen, and provides results that are specific only to that antigen. In addition, the product of Flamand appears to be only the pulsed dendritic cells.

In contrast, the present invention is directed to formulations comprising products of co-cultures between antigen presenting cells (APCs) and tumor cells. As discussed, for example, in the specification on page 4, lines 5-28, the present invention overcomes the shortcomings taught by methods reported in the art, such as those taught by Flamand. More specifically, the present invention obviates the need to identify specific antigens that elicit a CTL response. According to the present invention, all of the tumor antigens found in the utilized tumor cell are presented to the MHC class 1 restricted pathway through the antigen presenting cell by co-culturing the APCs with the tumor cells. This result is neither taught nor suggested by Flamand. Thus, the present invention does not require the isolation and identification of specific antigens, but rather uses a non-specific approach which provides protection against a spectrum of antigens found in the tumors co-cultured with the antigen presenting cells.

The Office Action characterizes Applicants' claims as being drawn to product by process claims. Applicants respectfully disagree with this characterization. All of the claims at issue recite either a formulation or a pharmaceutical composition comprising the products of co-culture between antigen presenting cells and either tumor

cells or virally infected cells. The term "products of co-cultures" is defined in the specification on page 8, lines 18-22, as the matter resulting from co-culture of APCs and, for example, tumor cells, and includes "cells that have become fused together, cells that are not fused, and cellular components including but not limited to the cytoplasm and nuclear matter released from the cell upon cell death or rupture or by other processes." The relevant claims therefore recite formulations or pharmaceutical compositions comprising such fused cells, nonfused cells and cellular components; it is submitted that the recited formulation and pharmaceutical composition are therefore not expressed in terms of product by process.

Even if the claims were product by process claims, which Applicants do not concede, Flamand is still not appropriately cited to reject those claims. The Office Action states, incorrectly, that "Applicant's disclosed method and the method of Flamand et al both result in the generation of the same product, dendritic cells which are loaded with tumor-specific antigen which can present antigen fragments to T cells for the purpose of activating a tumor-specific immune response." As noted above, Applicants and Flamand do not teach the same product. Flamand teaches methods of generating *dendritic cells* loaded with *a specific tumor antigen*. Applicants, in contrast, teach products of co-culture, as defined above, and not dendritic cells alone. In addition, the present products of co-culture are not loaded with a tumor-specific antigen but rather are incubated with *all* of the antigens present in the tumor cells with which they are incubated. As noted in the specification, page 4, lines 26-28, "By delivering the entire array of antigens produced by a tumor cell or a virally infected cell to the APCs, a mechanism is provided for broad, polyvalent immunization." As further noted on page 10, lines 15 and 16, "The methods of the present invention result in the induction of tumor specific lytic activity in an immunized mammalian host." Thus, Flamand teaches dendritic cells pulsed with one antigen. In contrast, the present invention is directed to an aglomeration of cells and cell components incubated with numerous antigens.

The Office Action "reminds" Applicants "that a product remains the same irrespective of the manner in which it is produced." Applicants note, however, that when a different process results in a different product, the different product can be patentable. Here, Applicants use a decidedly different process than that taught by Flamand; this is conceded in the Office Action. Furthermore, the different process results in an entirely different product, as clearly demonstrated above. In addition, the ratios recited in Claims 17-19 and 22-24 are not taught by the art; since Flamand does

not teach use of tumor cells or virally infected cells themselves it cannot teach the tumor cell: antigen present cell ratios recited in these claims.

The Office Action further indicates that Flamand teaches formulations of dendritic cells loaded with idiotype proteins specific to the BCL1 lymphoma cell as a pharmaceutical preparation which can be administered to mice prophylatically to protect them from a BCL1 lymphoma cell challenge. Flamand, however, does not teach the present pharmaceutical preparation. As discussed above, Flamand does not teach the products of co-cultures of antigen presenting cells with tumor cells or virally infected cells, and therefore cannot teach a pharmaceutical preparation which utilizes such a product. Again, Applicants' formulations do not comprise single APCs that are specific to only one antigen.

The Office Action also states that Flamand teaches the product of co-incubating B cells with antigen. Significantly, however, Flamand teaches that B cells *do not work* in their disclosed method. (See Abstract, "No such protection can be achieved when B cells are used as APC.") Thus, Flamand teaches away from use of B cells.

The Office Action cites the Unanue reference as allegedly providing "evidence that splenic dendriditic cells are the same as those found in lymph nodes and as the Langerhans cells of the skin . . . ." Similarly, the Dezutter-Dambuyant reference is cited as allegedly providing evidence "that these are also the same as the dermal dendritic cells and which arise from bone marrow precursors . . . ." Applicants disagree with these characterizations. The cited section of the Unanue reference states that the Langerhans dendritic cells, including the Langerhans cells of the skin, the "'veiled cells' of afferent lymphatics, the dendritic cells (DCs) of the spleen and some of the 'interdigitating cells' of the lymphoid organs" are "a family of related cells" (emphasis added), not "the same" as suggested by the Office Action. In addition, the abstract of the Dezutter-Damuyant reference does not appear to discuss splenic antigen-presenting cells. In any event, even if these references did teach the equivalence of splenic antigen presenting cells to other forms of APCs, which Applicants do not concede, they do not overcome the shortcomings of the Flamand reference.

Claims 13-15 and 17-24 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Mayordomo et al. as evidence by Unanue and Dezutter-Damuyant. This rejection is respectfully traversed. The comments made above regarding the Unanue and Dezutter-Damuyant references apply equally here.

The Mayordomo reference is just as irrelevant to the present products as the Flamand reference, if not more irrelevant. Mayordomo teaches pulsing of dendritic cells with tumor associated peptides. Like the Flamand reference, a specific peptide is utilized to modify the dendritic cell; the peptide is synthetically produced. The resulting dendritic cells elicit protective and therapeutic antitumor immunity against only the specific peptide with which they are pulsed. As with Flamand, the Mayordomo reference fails to teach a product which is effective against an array of antigens expressed by a tumor cell, and which is produced without requiring the isolation and identification of specific antigens or the synthesis of a specific antigen. The Office Action notes that the Mayordomo reference teaches that the vaccinated mice are only protected from a challenge by the specific tumor and not the broad array taught by Applicants. In addition, the Mayordomo reference fails to teach the product of co-cultures as recited in the present claims. Instead, single dendritic cells are taught. Thus, the present invention is patentable over the Mayordomo, Unanue, Dezutter-Damuyant combination for the same reasons that it is allowable over the Flamand, Unanue, Dezutter-Damuyant combination.

To establish anticipation under Section 102, every element of the claim must be present in a single reference. (See *Jamesbury Corporation v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985), a copy of which is enclosed.) Not every element of the products recited in Claims 13-15 and 17-24 are contained in either the Flamand or the Mayordomo references. More specifically, neither of the references teach formulations or pharmaceutical compositions comprising the products of co-culture of antigen-presenting cells and either tumor cells or virally infected cells. Rather, both references teach dendritic cells that have been pulsed with a specific antigen or peptide, and which elicit only specific immunity. In contrast, the products taught by Applicants are an agglomeration of cells and cell components having a broad array of immunological ability. Thus, the present invention is not appropriately rejected under 35 U.S.C. § 102(b) in light of the references either alone or in combination with the teachings of Unanue and Dezutter-Damuyant.

SUMMARY

For all of the above reasons, Applicants respectfully submit that Claims 13-15 and 17-24 are allowable over the art of record. A Notice of Allowance is therefore respectfully requested at an early date.

Respectfully submitted,

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